FIGURE LEGENDS:

Figure 1S: Relative abundance of transcripts encoding enzymes involved in lipid synthesis in HepG2 and LnCap cells. Quantitative RT-PCR was used to quantify expression levels of transcripts encoding enzymes involved in lipid metabolism. Primers used for qRT-PCR are listed in Table 1. Results are expressed as mRNA Abundance; Transcript/Cyclophilin. The average C_t value for cyclophilin in HepG2 and LnCap cells was 20.3 $\pm$ 0.5 and 19.7 + 0.3, respectively. Results are the mean $\pm$ S.D. three independent samples.

Figure 2S: Effect of Soraphen A and C75 on [2-^{14}C]-acetate metabolism in HepG2 cells. HepG2 cells grown to ~80% confluence in DMEM + 10% FBS were treated with DMSO, soraphen A (0.1 -1 μM) or C75 (50-200 μM) for 6 hours while cells received [2-^{14}C]-acetate (0.5 μCi/well, 6-well plate). After treatment, cells were harvested & extracted for total lipid (Materials & Methods). Total lipid was fractionated by thin layer chromatography & the distribution of ^{14}C in lipid fractions was quantified by phosphor image analysis. Lipid standards (cholesterol ester [18:1,n-9], triacylglycerol, [TAG, triolean], non-esterified fatty acids, [NEFA, 18:1,n-9], cholesterol, diacylglycerol [DAG, diolean] and polar lipid [phosphatidyl choline] were obtained from Nu-Chek Prep & Avanti Polar Lipids. Results are expressed as phosphor image units X 10^{-5} mean $\pm$ S.D., n=3.

Figure 3S: Effect of soraphen A and C75 on fatty acid synthesis, elongation and desaturation.

Panel A: ^{14}C-labeled lipids from Fig. 1S were saponified and quantified by RP-HPLC & β-scintillation counting. ^{14}C was recovered in the following fatty acids: myristate (14:0), palmitoleate (16:1,n-7), palmitate (16:0), vaccenate (18:1,n-7) & oleate (18:1,n-9), stearate

(18:0). Results are reported as counts per second, CPS, mean ± SD, n=4.

Panel B. Desaturation & Elongation Index. The desaturation index was calculated by summing the ^{14}C-CPS in [16:1,n-7 + 18:1,n-7 + 18:n-9] & dividing by the sum of ^{14}C-CPS in [14:0 + 16:0 + 18:0]. The elongation index was calculated by summing the ^{14}C-CPS in [18:0 + 18:1,n-7 + 18:1,n-9] & dividing by the sum of ^{14}C-CPS in [16:0 + 16:1,n-7]. Mean ± SD, n=4; *, P<0.05 versus DMSO.

Figure 4S. Effect of elevated FADS1 and FADS2 expression on [1-^{14}C]-18:2,n-6 metabolism in HepG2 cells. HepG2 cells were infected with Ad-Luc, Ad-FADS1, Ad-FADS2 or Ad-FADS1 + Ad-FADS2 at 20 PFU/cell 48 hrs before fatty acid treatment. Cells were treated with 50 μM ^{14}C-linoleate for 6 hrs. Cells were harvested for total lipid extraction and saponification for RP-HPLC fractionation and quantitation of ^{14}C-linoleate elongation & desaturation products. Results are reported as % Distribution of ^{14}C in fatty acids; mean ± range of 2 separate studies. *. P<0.05 Ad-Luc vs Ad-FADS2 or Ad-FADS1 & 2, ANOVA.

Figure 5S: Effect of elevated elongase activity on *de novo* lipogenesis. HepG2 cells at ~80% confluence were infected with recombinant adenovirus expressing luciferase (Ad-Luc), fatty acid elongase-5 (Ad-Elovl5) or fatty acid elongase-6 (Ad-Elovl6) at 20 PFU/cell for 48 hrs before metabolic labeling with ^{14}C-acetate. An adenovirus expressing green fluorescent protein (Ad-GFP) was used to establish that at 20 PFU/cells, >90% of these cells express GFP. Cells were treated with [2-^{14}C]-acetate in the presence of DMSO. Six hours after [2-^{14}C]-acetate addition, lipids were extracted and fractionated by TLC. The distribution of ^{14}C into polar lipids, diacylglycerol (DAG), cholesterol, non-esterified fatty acids (NEFA), triacylglycerol (TAG) and cholesterol esters (Chol Est) derived from DMSO treated cells.

Figure 6S: Soraphen A, but not elevated Elovl5 or Elovl6 expression, increases fatty acid oxidation in HepG2 cells. HepG2 cells were treated with 50 μM [1-^{14}C]-palmitate [**Panels A**] or [1-^{14}C]-linoleate [**Panels B**] and DMSO or soraphen A (1 μM). After 6 hrs of treatment, media was collected for analysis of fatty acid oxidation products (Methods). Fatty acid oxidation results are expressed as: nmoles CO_2. Results are reported as mean ± SD, n=4, *. P<0.05 vs DMSO, t-test.